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EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 11/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/622,635	KALLIONIEMI ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22,24-63,66-78 and 86-102* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22 24-63 66-78 86-102* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ ~~Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)~~ Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. 1102
5) ☐ ~~Notice of Informal Patent Application (PTO-152)~~
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 27 August 2004 in which claims 6, 13, 16, 32, 58 were amended, claims 64-65 were canceled and claims 95-102 were added. All of the amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 28 April 2004, not reiterated below, are withdrawn in view of the amendments and/or Applicant's comments regarding Provisional Application 60/043,683, Stapleton et al. The previous rejections under 35 U.S.C. 102 and 35 U.S.C. 103, as reiterated below, are maintained. Applicant's arguments have been thoroughly reviewed and are discussed below. New grounds for rejection, necessitated by amendment, are discussed.

Claims 1-22, 24-63, 65-78 and 86-102 are under prosecution.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the

international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 1, 2, 4, 6, 7, 13, 15 and 88 are rejected under 35 U.S.C. 102(b) as being anticipated by Lampkin et al (Journal of Histotechnology, 1990, 13(2): 121-123.

Regarding Claim 1, Lampkin et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (base mold), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations, performing analysis of each copy and comparing the results of the analysis e.g. identification (page 122, left column, first and second full paragraphs and right column second full paragraph).

Regarding Claim 2, Lampkin et al disclose the method wherein the donor specimen is obtaining by boring (i.e. punched) an elongated sample from the specimen (paragraph bridging pages 121-122).

Regarding Claim 4, Lampkin et al disclose the method wherein the donor specimen is from a population of cells i.e. tissue (paragraph bridging pages 121-122).

Regarding Claim 6, Lampkin et al disclose the method wherein placing the donor specimen in an assigned location comprises forming an elongated receptacle in a donor block (Fig. 1D), obtaining an elongated specimen and obtaining a plurality of copies by sectioning the array transverse to the donor specimen (page 122, left column, first and second full paragraphs and Fig. 1).

Regarding Claim 7, Lampkin et al disclose the method wherein the donor specimen is placed in a receptacle having a size and shape "complementary" to the size and shape of the specimen (page 122, left column, first and second full paragraphs and Fig. 1). Lampkin teaches the donor specimens are placed into a grid-like base mold. Because the specimens are placed in grid-like mold, the grid is deemed to have size and shape "complementary" to the specimens.

Regarding Claim 13, Lampkin et al disclose the method wherein the sample is a tissue specimen (paragraph bridging pages 121-122).

Regarding Claim 15, Lampkin et al disclose the method wherein placing the specimen comprises placing a sample in a "corresponding" position of the multiple copies i.e. the samples are aligned relative to the sectioned arrays (page 122, left column, first and second full paragraphs and Fig. 1).

Regarding Claim 88, Lampkin et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (base mold), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations, performing analysis of each copy and comparing the results of the analysis e.g. identification (page 122, left column, first and second full paragraphs and right column second full paragraph).

Response to Arguments

4. Applicant asserts that Lampkin does not teach analysis in corresponding location of different copies to determine correlations at different locations. The argument has been considered but not found persuasive because the claims are broadly drawn to "analysis" which encompasses visual observations of two samples. Lampkin clearly observes the arrayed samples as illustrated in Fig. 1. Furthermore, Lampkin specifically teaches their sample blocks are cut into several hundred sections (i.e. providing substantial copies) and staining with "a variety of histochemical or immunocytochemical reagents (page 122, second full paragraph).

Applicant argues that Lampkin contains no description of comparing and correlating results. The argument has been considered but not found persuasive for the reasons stated above i.e. the claims analysis encompasses the visual observation as illustrated by Lampkin (Fig. 1).

Applicant further argues that Lampkin does not teach placing an elongated donor specimen in an elongated receptacle, but instead teaches alignment in a base mold which is then embedded in paraffin. The argument has been considered but is not found persuasive because, as Applicant acknowledges, Lampkin places the specimens in a base mold, which as illustrated (Fig 1D) meets the "elongated receptacle" requirement of Claim 6.

5. Claims 1-7, 9-15, 49 and 88 are rejected under 35 U.S.C. 102(b) as being anticipated by Kraaz et al (Journal of Clinical Pathology, 1988, 41: 1337).

Regarding Claim 1, Kraaz et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (warm cast), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations, performing analysis of each copy and comparing the results of the analysis i.e. immunostained and analyzed (center column and Fig. 1).

Regarding Claim 2, Kraaz et al disclose the method wherein the donor specimen is obtaining by boring (i.e. punched) an elongated sample from the specimen (center column, lines 1-7).

Regarding Claim 3, Kraaz et al disclose the method wherein the specimen is from a tumor (center column).

Regarding Claim 4, Kraaz et al disclose the method wherein the donor specimen is from a population of cells i.e. tissue (center column, lines 1-7).

Regarding Claim 5, Kraaz et al disclose the method wherein the donor specimen is from a cytological preparation i.e. tissue (center column, lines 1-7).

Regarding Claim 6, Kraaz et al disclose the method wherein placing the donor specimen in an assigned location comprises forming an elongated receptacle in a donor block (i.e. cast), obtaining an elongated specimen and obtaining a plurality of copies by sectioning the array transverse to the donor specimen (center column and Fig. 1).

Regarding Claim 7, Kraaz et al disclose the method wherein the donor specimen is placed in a receptacle having a size and shape "complementary" to the size and shape of the specimen (center column and Fig. 1). Kraaz teaches the donor specimen is placed into a cast. Because the specimens are placed in cast, the grid is deemed to have a size and shape "complementary" to the specimens.

Regarding Claim 9, Kraaz et al disclose the method further comprising associating a clinical characteristic with each assigned location i.e. each tumor specimen is assigned a position (center column, lines 1-7).

Regarding Claim 10, Kraaz et al disclose the method wherein a different analysis is performed on each array (center column, last paragraph).

Regarding Claim 11, Kraaz et al disclose the method wherein the analysis is immunological analysis (center column and Fig.. 1).

Regarding Claim 12, Kraaz et al disclose the method further comprising determining whether there are "correlations" between clinical characteristic "associated" with each location i.e. the tumor specimens are compared to controls (center column, second full paragraph).

Regarding Claim 13, Kraaz et al disclose the method wherein the sample is a tissue specimen (center column, lines 1-7).

Regarding Claim 14, Kraaz et al disclose the method wherein clinical characteristics are determined apart from array analysis and the characteristics are tumor grade, size or status i.e. various degrees of reactivity (center column, second full paragraph).

Regarding Claim 15, Kraaz et al disclose the method wherein placing the specimen comprises placing a sample in a "corresponding" position of the multiple copies i.e. the samples are aligned relative to the sectioned arrays (center column, lines 1-7).

Regarding Claim 49, Kraaz et al disclose the method wherein donor specimens are from one or more tumors (center column).

Regarding Claim 88, Kraaz et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (warm cast), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations, performing analysis of each copy and comparing the results of the analysis i.e. immunostained and analyzed (center column and Fig. 1).

Response to Arguments

6. Applicant asserts that Kraaz does not teach analysis in corresponding location of different copies to determine correlations at different locations. The argument has been considered but not found persuasive because the claims are broadly drawn to "analysis" which encompasses visual observations of two samples. Kraaz clearly observes the arrayed samples as illustrated in the figure.

Applicant further argues that Kraaz does not teach placing an elongated donor specimen in an elongated receptacle, but instead teaches placing the specimens in a cast of melted paraffin. The argument has been considered but is not found persuasive because, as Applicant acknowledges, Kraaz places the specimens in a cast, which as illustrated in the figure, meets the "elongated receptacle" requirement of Claim 6.

7. Claims 1-20, 29-30, 43-44, 49, 53-61, 70, 87-92, 95-97, 101 and 102 are rejected under 35 U.S.C. 102(b) as being anticipated by Enghardt et al (Journal of Histotechnology, 1995, 18(1): 51-55).

Regarding Claim 1, Enghardt et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (cassette, and page 55, second full paragraph), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations (page 53, right column "slides"), performing analysis of each copy and comparing the results of the analysis i.e. immunostained and analyzed (page 53, last paragraph-page 54, left column).

Regarding Claim 2, Enghardt et al disclose the method wherein the donor specimen is obtaining by boring (i.e. punched) an elongated sample from the specimen (page 53, paragraph spanning left to right column).

Regarding Claim 3, Enghardt et al disclose the method wherein the specimen is from a tumor (Fig. 3).

Regarding Claim 4, Enghardt et al disclose the method wherein the donor specimen is from a population of cells i.e. tumor tissue (Fig. 3).

Regarding Claim 5, Enghardt et al disclose the method wherein the donor specimen is from a cytological preparation i.e. tumor cells (Fig. 3).

Regarding Claim 6, Enghardt et al disclose the method wherein placing the donor specimen in an assigned location comprises forming an elongated receptacle in a donor block (page 52, right column), obtaining an elongated specimen (page 53, right column) and obtaining a plurality of copies by sectioning the array transverse to the donor specimen (page 53, right column, "slides" and Fig. 2).

Regarding Claim 7, Enghardt et al disclose the method wherein the donor specimen is placed in a receptacle having a size and shape "complementary" to the size and shape of the specimen (page 52, right column and page 53, right column).

Regarding Claim 8, Enghardt et al disclose the method wherein forming the elongated receptacle comprises forming a cylindrical bore in the recipient block and the donor specimen is obtained by boring a cylindrical tissue specimen from the donor block wherein the diameters of the receptacle and donor are substantially the same (pages 52-53).

Regarding Claim 9, Enghardt et al disclose the method further comprising associating a clinical characteristic with each assigned location i.e. diagnosis (page 55, first paragraph).

Regarding Claim 10, Enghardt et al disclose the method wherein a different analysis is performed on each array (page 54, left column and page 52, Table 1).

Regarding Claim 11, Enghardt et al disclose the method wherein the analysis is immunological analysis (page 54, left column and page 52, Table 1).

Regarding Claim 12, Enghardt et al disclose the method further comprising determining whether there are correlations between clinical characteristics associated with each location (page 55, left column).

Regarding Claim 13, Enghardt et al disclose the method wherein the sample is a tissue specimen (Fig. 3).

Regarding Claim 14, Enghardt et al disclose the method wherein clinical characteristics are determined apart from array analysis and the characteristics are tumor grade, size or status i.e. diagnosis (page 55, first paragraph).

Regarding Claim 15, Enghardt et al disclose the method wherein placing the specimen comprises placing a sample in a "corresponding" position of the multiple copies i.e. the samples are aligned relative to the sectioned arrays (page 55).

Regarding Claim 16, Enghardt et al disclose a method of parallel analysis of biological specimens comprising forming a donor block comprising a biological specimen embedded in

embedding medium (page 51, right column and page 53) obtaining a plurality of donor specimens cores (page 53), boring recipient cores from recipient embedding medium form an array of elongated receptacles (page 52, right column) placing each donor cores in the elongated receptacles at assigned locations (page 53) seconding the recipient embedding medium transverse to the elongated receptacles (page 53 "slides") performing different biological analysis on each cross-section and comparing the results to determine correlations (page 53, last paragraph-page 54, left column).

Regarding Claim 17, Enghardt et al disclose the method further comprising comparing the results to clinical information about the specimen (page 54, left column and Fig. 3).

Regarding Claim 18, Enghardt et al disclose the method wherein the specimen is from a tumor (Fig.3).

Regarding Claim 19, Enghardt et al disclose the method wherein the analysis is immunological analysis (page 54, left column and page 52, Table 1).

Regarding Claim 20, Enghardt et al disclose the method further comprising comparing the results to clinical information about the subject from whom the specimen was obtained (page 55, left column and Fig. 3).

Regarding Claim 29-30, Enghardt et al disclose the method wherein the comparing comprises determination of protein expression by immunological analysis (Table 1 and page 53-54).

Regarding Claims 43-44, Enghardt et al disclose the method wherein the analyzing evaluates a reagent for diagnosis i.e. antibody (Fig. 3).

Regarding Claim 49, Enghardt et al disclose the method wherein donor specimens are from one or more tumors (Fig.3).

Regarding Claim 53, Enghardt et al disclose a method of analyzing cellular specimens in a matrix with specimens positioned at predetermined known locations such that multiple copies of the matrix are provided in a two dimensional array, the method comprising exposing

sequential copies of the matrix to an agent which interacts with the specimens to identify specimens which share a biological property i.e. antibody binding (pages 53-54).

Regarding Claim 54, Enghardt et al disclose the method wherein the specimens are provided in an elongated form and multiple copies are made by sectioning from a three dimensional array such that sequential section maintain a predetermined relationship (page 52, right column and page 53, right column).

Regarding Claim 55, Enghardt et al disclose the method wherein the shared biological property is a molecular characteristic i.e. antibody binding partner (Table 1 and pages 53-54).

Regarding Claim 56, Enghardt et al disclose the method wherein the shared biological property is presence of a protein (Table 1).

Regarding Claim 57, Enghardt et al disclose the method wherein the property is a specific reaction with an antibody specific for a specimen of interest (Table 1).

Regarding Claim 58, Enghardt et al disclose the method wherein the property is "correlated" with an other characteristic of the specimens (Table 1). As stated above, the claim is unclear because "other characteristic" is not defined or described. Additionally, the claim language "correlated" is very broad and interpreted thusly. As such, the protein expression and antibody binding are two characteristics analyzed by Enghardt that meet the limitations of the claim.

Regarding Claim 59, Enghardt et al disclose the method wherein the property includes clinical information about the subject i.e. diagnosis (page 55, left column).

Regarding Claim 60, Enghardt et al disclose the method wherein clinical information includes tumor grade, size or status i.e. diagnosis (page 55, first paragraph).

Regarding Claim 61, Enghardt et al disclose the method wherein the specimen is a tissue specimen (Fig.3).

Regarding Claim 70, Enghardt et al disclose the method wherein the specimens comprise animal cells i.e. tissue cells (Fig. 3).

Regarding Claim 87, Enghardt et al disclose the method wherein the method does not destroy the morphology of the specimen (page 51, right column).

Regarding Claim 88, Enghardt et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (cassette, and page 55, second full paragraph), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations (page 53, right column "slides"), performing analysis of each copy and comparing the results of the analysis i.e. immunostained and analyzed (page 53, last paragraph-page 54, left column).

Regarding Claim 89, Enghardt et al disclose the method of Claim 1 further comprising correlating information concerning the specimen with the analysis wherein the information includes tumor grade, size or status i.e. diagnosis (page 55, first paragraph).

Regarding Claim 90, Enghardt et al disclose a method of parallel analysis of biological specimens comprising forming a donor block comprising a biological specimen embedded in embedding medium (page 51, right column and page 53) obtaining a plurality of donor specimens cores (page 53), boring recipient cores from recipient embedding medium form an array of elongated receptacles (page 52, right column) placing each donor cores in the elongated receptacles at assigned locations (page 53) seconding the recipient embedding medium transverse to the elongated receptacles (page 53 "slides") performing analysis on each cross-section and determining frequency (i.e. plus or minus binding) of antibody binding (page 53, last paragraph-page 54, left column).

Regarding Claim 91, Enghardt et al disclose the method further comprising obtaining donor specimens from a predetermined morphologically defined region of a tumor (e.g. controls and lymph nodes (page 53, left column and Fig. 3).

Regarding Claim 92, Enghardt et al disclose the method further comprising obtaining donor specimens from a predetermined cell structure (e.g. controls and lymph nodes (page 53, left column and Fig. 3).

Regarding Claim 95, Enghardt et al disclose the method wherein a first biological analysis is performed on a first copy (control multitissue array) and a second analysis on a second copy wherein the first and second analysis are different i.e. different antibodies (page 54, left column).

Regarding Claim 96, Enghardt et al disclose the method wherein different analysis comprises a first biological analysis on a first cross section (control multitissue array) and a second analysis on a second cross section i.e. different antibodies on multiple control arrays (page 54, left column).

Regarding Claim 97, Enghardt et al disclose the method comprising exposing a first sequential copy (control array) to a first agent (antibody) and a second copy to a second and different agent i.e. different antibodies on multiple control arrays (page 54, left column).

Regarding Claims 101 and 102, Enghardt et al disclose the methods of Claims 1 and 6 comprising preparing copies of the array and comparing results of the biological analysis to determine correlations between the results as each location i.e. Enghardt prepares multitissue arrays, exposes them to multiple antibodies and compares the results to determine, at least, edge affects and background (page 54, "Results).

Response to Arguments

8. Applicant asserts that Enghardt does not teach analysis in corresponding location of different copies to determine correlations at different locations and there is no explicit description that results in corresponding analysis as claimed. The argument has been considered but not found persuasive because, as stated above, the claims are broadly drawn to "analysis" which encompasses visual observations of two samples. Enghardt teaches

immunostaining and comparisons between multitissue controls and patient samples (page 54, left column). Hence, Enghardt clearly observation and analysis as claimed.

Applicant asserts that Enghardt does not teach performing different analysis on each copy or comparing result to determine correlations as per Claims 10, 16 and 90. The argument has been considered but not found persuasive because, as stated above, the correlations are not limited to any specific techniques and as such are encompassed by any observation and/or analysis technique. Enghardt provide multiple copies of multitissue control arrays (page 53, right column) and using twelve monoclonal antibodies compares a multitissue control array to patient tissue array (page 53, right column-page 54, left column).

Applicant asserts that Enghardt does not teach exposing sequential copies as required by Claim 53. The argument has been considered but is not found persuasive because a sited above, Enghardt provides sequential copies of control multitissue blocks for immunostaining. Hence, they meet the requirements of Claim 53.

Applicant further argues that Enghardt does not include any mention of such utilization of clinical characteristics e.g. (Claim 12)"determining whether there are correlations between clinical characteristics, associated with each assigned location, and the different biological analysis"; (Claim 14) "the clinical characteristics are determined apart from performing the different biological analysis of each copy of the array; and the characteristics are one or more of patient age, tumor grade, tumor size, node status, and receptor status." Applicant asserts that a general diagnosis (as cited in the rejection) is not correlated with any biological analysis. The argument has been considered but is not found persuasive because, as noted above, the claims are broadly drawn to results in "corresponding" locations to determine "correlations" between analysis. The broad claim language does not define or limit the technique of analysis or comparison, but instead encompasses any simple analysis. As cited in the office action, Enghardt compares the analysis and from the comparison provides a diagnosis. While Enghardt does not describe the technique used to provide the diagnosis, the

claims are so broadly drawn as to encompass any technique. Hence, Enghardt teaches the analysis as claimed.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 21, 22, 45-48, 93-94 and 98-100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Enghardt et al (Journal of Histotechnology, 1995, 18(1): 51-55)

Regarding Claims 21, 93 and 94, Enghardt et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (cassette, and page 55, second full paragraph), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations (page 53, right column "slides"), performing analysis of each copy and comparing the results of the analysis i.e. immunostained and analyzed (page 53, last paragraph-page 54, left column) and further comprising obtaining donor specimens from a predetermined morphologically defined region of a tumor (e.g. controls and lymph nodes (page 53, left column and Fig. 3) and further comprising obtaining donor specimens from a predetermined cell structure (e.g. controls and lymph nodes (page 53, left column and Fig. 3).

Enghardt et al teach the method wherein the tissue section and block are maintained in close proximity for easy association between them (page 55, left column) but they do not teach alignment of the section above the donor block for tissue identification. However, it would have been obvious to one of ordinary skill in the art, having both the donor block and tissue section in close proximity, to align the two, one above the other, for convenient identification.

Regarding Claims 22 and 98-100, Enghardt et al disclose the method wherein the donor core is substantially cylindrical and has a diameter of "about" 1mm(page 53). Enghardt et al do not teach a diameter of less than 1mm (or 0.3 to 2.0) and a length of 1 to 4 mm. However, the courts have stated that claimed dimensions of a known device do not distinguish over the prior art device when the claimed device would not perform differently from the prior art device. *In Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), cert. denied, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device. Therefore, the instantly claimed dimensions would have been an obvious variation of the dimensions of Enghardt et al.

Regarding Claim 45-48, Enghardt et al teach the method wherein analysis specifically includes reagent analysis, quality control and analysis of differentiation (page 55, left column). They do not teach the intended uses recited in Claims 45-48. However, one of ordinary skill in the art would have been motivated to apply the method of Enghardt et al for claimed uses based on tissue being examined and anticipated diagnosis.

Response to Argument

11. Applicant assets the examiner has relied on impermissible hindsight because Enghardt does not refer to any proper motivation in the reference for aligning the tissue above the donor block as per Claim 21. In response to applicant's argument that the examiner's conclusion of

obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

12. Claims 24-29, 31, 50-52, 62-63, 68-69, 71-78 and 86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Enghardt et al (Journal of Histotechnology, 1995, 18(1): 51-55) in view of Stapleton et al (U.S. Patent No. 6,103,192, issued 15 August 2000).

Regarding Claims 24-29 and 31, Enghardt et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (cassette, and page 55, second full paragraph), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations (page 53, right column "slides"), performing analysis of each copy and comparing the results of the analysis i.e. immunostained and analyzed (page 53, last paragraph-page 54, left column).

Enghardt et al do not teach using a nucleic acid array to identify a biomarker. However, nucleic acid array identification of biomarkers was well known in the art at the time the claimed invention was made as taught by Stapleton et al (Column 1, lines 20-40).

Stapleton et al teach a similar method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (matrix) and performing analysis of the specimens using

a nucleic acid microarray (Column 1, lines 20-40) wherein the marker is selected by genetic analysis; wherein the marker is for gene expression and altered gene expression in for various tumor and diagnostic analysis (Column 6, lines 1-25; Column 16, lines 15-18; and Example 7). Stapleton et al further teach a motivation for using the microarray analysis i.e. minimizes the amount of specimen required for analysis and eliminates the need to extract nucleic acids from the sample (Column 5, lines 1-5 and 33-37).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the nucleic acid microarray analysis of Stapleton et al to the specimen analysis of Enghardt et al for the expected benefits of inexpensive, rapid and sensitive diagnosis of clinically important tumors at the nucleic acid level as taught by Stapleton et al (Column 5, lines 1-48).

Regarding Claims 50-52 and 86, Enghardt et al teach the method wherein a plurality of different tumor tissues are analyzed but they do not specifically teach breast, bladder or prostate tumors, or from a plurality of tumors of the same type. However, Stapleton et al teach the similar method wherein the specimen is breast and/or from plurality of tumors of the same or different type and wherein the method is applicable to any tissue (Column 6 and Example 5). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the tumor specimens of Enghardt and Stapleton by analyzing different specimens of the same tissue e.g. breast, prostate or bladder for the obvious benefits of comparative analysis of normal and patient specimens as taught by Stapleton (Column 6, lines 15-25).

Regarding Claim 62-63, 68-69, 71-78, Stapleton et al teach their method wherein the cellular specimen is a cellular suspension that has been converted into a solid specimen (Column 9, line 61-Column 10, line 14) and wherein the suspension is from a body fluid e.g. malignancy from one or more cell lines and immobilized on a support (Column 11, line 27-Column 12, line 50). It would have been obvious to one of ordinary skill in the art at the time

the claimed invention was made to modify the tissue cells of Enghardt et al with clinically important cell suspensions as taught by Stapleton et al for the obvious benefits of inexpensive, rapid and sensitive diagnosis of clinically important specimens at the nucleic acid level as taught by Stapleton et al (Column 5, lines 1-48). Stapleton further teach the method wherein normal tissues are compared to patient tissues (Column 6, lines 20-25) but they do not specifically teach the normal tissues are from a model organism or at different stages of tumor progression. However, it would have been further obvious to analyze tumors from a model organism and/or at different stages of progression for the obvious benefits of providing a stage-specific analysis and subsequently providing stage-specific treatment based on the analysis.

Response to Arguments

13. Applicant asserts that Stapleton reference is not prior art for the above claims because the provisional application of Stapleton (filed, 14 April 1997) does not contain the passage cite in the office action for comparing sequences to sequences from different specimens. Applicant's arguments have been considered. It is acknowledged that the provisional application does not contain the cited passage. However, the provisional application of Stapleton clearly and repeatedly teaches parallel analysis. For example, at page 25, Example 6, the provisional application teaches comparison of arrayed samples. Applicant further assets that the provisional application does not teach an array of nucleic acids. The assertion is noted. However, the instant claims are broadly drawn to microarray, but do not define or limit the microarray structurally so as to define the microarray over the arrayed samples of Example 6 or the arrayed (electrophoresed) fragments illustrated in Fig. 1-6. Applicant asserts that the instantly claimed microarray is defined over the teaching of Stapleton in the instant specification (page 9). The cited passage merely reads: "A "microarray" is an array that is miniaturized so as to require microscopic examination for visual evaluation." While the claims are read in light of the specification, limitations from the specification are not read into the claims. Furthermore, the instantly claimed microarray is not supported by Applicant's

provisional application filed 25 February 1998. For all the reasons stated above, Stapleton is a prior art reference and teaches the elements missing from the teachings of Enghardt.

Applicant acknowledges the probe array of Stapleton, but asserts that the passage does not constitute a teaching of the array because they only describe detecting mutations from a single sample. The argument has been considered but is not found persuasive to overcome the instant rejection because Stapleton is relied upon for knowledge of one having ordinary skill. Stapleton teaches the elements missing in the teaching of Enghardt as known in the art and provides the essential motivation for combining the teachings.

Applicant argues that Stapleton and Enghardt do not teach expression of specific proteins. The argument has been considered but not found convincing to overcome the above rejection because Stapleton teaches expression analysis in samples of interest (Column 5, lines 1-32) and Enghardt also teaches expression analysis in samples of interest (page 51, left column). While they do not specifically teach analysis of the claimed proteins, absent unexpected results, it would have been obvious to one of ordinary skill to analyze the claimed proteins based on the samples being analyzed and their known expression pattern in diseased versus normal tissues as suggested by Enghardt and Stapleton.

14. Claims 32-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stapleton et al (U.S. Patent No. 6,103,192, issued 15 August 2000) in view of An et al (U.S. Patent No. 5,882,864, issued 16 March 1999).

Regarding Claim 32, Stapleton et al disclose the method of analyzing genetic changes and gene expression in a tissue specimen the method comprising screening multiple genes with a nucleic acid array and screening multiple biological specimens in a specimen array (matrix) with a nucleic acid probe (primer) to detect genes which are abnormally expressed wherein the results of specimen screening is used to detect the array (Column 16, lines 9-28) but they do

not teach the screening is used to select an array. However, An et al teach a similar method of tissue specimen analysis wherein the analysis provides disease-specific probes for diagnosis of tumors (Column 2, line 56-Column 3, lines 9). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the probe selection of An et al to the method of Stapleton et al to thereby select the arrayed probes from their screening step for the expected benefit of providing an array of disease-specific probes for diagnosis of tumors as taught by An et al (Column 2, line 56-Column 3, lines 9).

Regarding Claims 33-34, Stapleton et al disclose the method wherein the screening comprises high throughput genomic technique i.e. oligonucleotide arrays (Column 16, lines 9-36).

Regarding Claim 35, Stapleton et al teach the method wherein screening comprises searching database or other biomedical information sources as exemplified by their primer selection/design based on known sequences (Column 5, lines 61-63; Column 11, lines 30-37; and Example 1: Column 16, line 64-Column 17, line 22).

Regarding Claim 36, Stapleton et al teach the method wherein the screening comprises using a probe array (Column 16, lines 9-28) and they further teach their method detects mRNAs (Column 6, lines 11-25). While they do not specifically teach their probe arrays are cDNA arrays, it would have been obvious to one of ordinary skill in the art that probe arrays for mRNA detection comprise cDNAs. Therefore, one of ordinary skill in the art would have been motivated to apply cDNA arrays to the method of Stapleton for the obvious benefit of analyzing mRNA populations as Stapleton et al desires (Column 6, lines 11-25).

Regarding Claim 37, Stapleton et al disclose the method wherein the screening comprises an array that is assayed for mutation (Column 16, lines 9-59).

Regarding Claim 38, Stapleton et al disclose the method wherein the array comprises loci that undergo differential expression in cancer (Example 7).

Regarding Claim 39, Stapleton et al disclose the method wherein the screening comprises hybridizing nucleic acids associated with a cell with the array and determining which loci indicate differential expression (Column 5, lines 33-48; Column 16, lines 9-59; and Example 7). An et al teach the similar method of probe screening (Fig. 1-15).

Regarding Claim 40, Stapleton et al disclose the method further comprising selecting a target that undergoes differential expression and using the probe to screen the specimens (Column 5, lines 33-48; Column 16, lines 9-59; and Example 7). An et al teach the similar method of probe selection (Claim 2).

Regarding Claim 41-42, Stapleton et al disclose the method wherein the specimen is a tumor specimen (Column 6, lines 1-25) and An et al teach the tumor specimen (Fig. 1-15).

Response to Arguments

15 Applicant relies on the arguments discussed above regarding Stapleton and Enghardt and Applicant asserts that An does not teach the lacking elements. Those arguments have not been found persuasive as discussed above.

16. Claims 66 and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Enghardt et al (Journal of Histotechnology, 1995, 18(1): 51-55) in view of Stapleton et al (U.S. Patent No. 6,103,192, issued 15 August 2000) and An et al (U.S. Patent No. 5,882,864, issued 16 March 1999).

Regarding Claims 66 and 67, Enghardt et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (cassette, and page 55, second full paragraph), obtaining a plurality of copies of the recipient array such that the copies maintain

their assigned locations (page 53, right column "slides"), performing analysis of each copy and comparing the results of the analysis i.e. immunostained and analyzed (page 53, last paragraph-page 54, left column).

Enghardt et al do not teach using a nucleic acid array to identify a biomarker. However, nucleic acid array identification of biomarkers was well known in the art at the time the claimed invention was made as taught by Stapleton et al (Column 1, lines 20-40).

Stapleton et al teach a similar method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (matrix) and performing analysis of the specimens using a nucleic acid microarray (Column 1, lines 20-40) wherein the marker is selected by genetic analysis; wherein the marker is for gene expression and altered gene expression in for various tumor and diagnostic analysis (Column 6, lines 1-25; Column 16, lines 15-18; and Example 7). Stapleton et al further teach a motivation for using the microarray analysis i.e. minimizes the amount of specimen required for analysis and eliminates the need to extract nucleic acids from the sample (Column 5, lines 1-5 and 33-37).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the nucleic acid microarray analysis of Stapleton et al to the specimen analysis of Enghardt et al for the expected benefits of inexpensive, rapid and sensitive diagnosis of clinically important tumors at the nucleic acid level as taught by Stapleton et al (Column 5, lines 1-48).

Enghardt et al and Stapleton do not teach their screening is used to select a probe for an array. However, An et al teach a similar method of tissue specimen analysis wherein the analysis provides disease-specific probes for diagnosis of tumors and specifically her-2 analysis (Column 2, line 56-Column 3, lines 9 and Claim 2). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the probe selection and her-2 analysis of An et al to the method of Enghardt et al and Stapleton et al to

thereby select the arrayed probes from their screening step for the expected benefit of providing an array of disease-specific probes for diagnosis of tumors as taught by An et al (Column 2, line 56-Column 3, lines 9).

Response to Arguments

17. Applicant relies on the arguments discussed above regarding Stapleton and Enghardt and Applicant asserts that An does not teach the lacking elements. Those arguments have not been found persuasive as discussed above.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

19 No claim is allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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Art Unit: 1634
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